Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- 1. (currently amended) A computer implemented method to search a heterogeneous heterogeneous compound database composed of molecules from different sources and syntheses, some known and some unknown, for molecules which are likely to have the same biological activity as a known query molecule comprising the following steps:
 - a) fragmenting a query molecule and database molecules according to a defined set of rules;
 - b) generating shape descriptors for the query molecule fragments and for the database molecules fragments; and
 - c) using the shape descriptors, comparing all combinations of query molecule fragments with database molecule fragments for each database molecule to identify identifying the database molecule which has a shape similar to the query molecule; and
 - d) outputting the identity of the database molecule.
- 2. (currently amended) A computer implemented method to search a <u>heterogeneous</u> heterogeneous compound database composed of molecules from different sources and syntheses, some known and some unknown, for molecules which are likely to have the same biological

activity as a known query molecule comprising the following steps:

- a) fragmenting a query molecule according to a defined set of rules;
- b) topomerically aligning the query molecule fragments to generate a topomeric conformation;
- c) generating the interaction energies between a probe and the atoms in the topomerically aligned query fragments at all intersection points in a three dimensional grid surrounding the aligned query fragments;
- d) fragmenting a database molecule according to a defined set of rules;
- e) topomerically aligning the database molecule fragments to generate a topomeric conformation;
- f) generating the interaction energies between a probe and the atoms in the topomerically aligned database molecule fragments at all intersection points in a three dimensional grid surrounding the aligned database molecule fragments;
- g) determining the similarity between query fragments and database molecule fragments by the root sum square differences in the field values; and
- h) identify the molecule in the database most similar to the query molecule as that molecule having the smallest field value difference in its fragments; and
- i) outputting the identity of the database molecule.
- 3. (currently amended) A computer implemented method to search a <u>heterogeneous</u> heterogeneous compound database composed of molecules from different sources and syntheses,

some known and some unknown, for molecules which are likely to have the same biological activity as a known query molecule comprising the following steps:

- a) fragmenting a query molecule according to a defined set of rules;
- b) topomerically aligning the query molecule fragments to generate a topomeric conformation;
- c) generating the interaction energies between a probe and the atoms in the topomerically aligned query fragments at all intersection points in a three dimensional grid surrounding the aligned query fragments;
- d) assigning features locations in the topomerically aligned query fragments;
- e) fragmenting a database molecule according to a defined set of rules;
- f) topomerically aligning the database molecule fragments to generate a topomeric conformation;
- g) generating the interaction energies between a probe and the atoms in the topomerically aligned database molecule fragments at all intersection points in a three dimensional grid surrounding the aligned database molecule fragments;
- h) assigning features locations in the topomerically aligned database molecule fragments;
- i) determining the similarity between query fragments and database molecule fragments by the root sum square differences in the field values;
- j) identifying all database molecule fragments which have features, similarly located

in topomer space and similar in feature property, that match each feature in the query fragments; and

- k) identifying the molecule in the database most similar to the query molecule as that molecule having the smallest field value difference in its fragments and smallest difference in features molecule; and
- d) outputting the identity of the database molecule.
- 4. (previously presented) The method of claim 3 in which the feature contributions are weighted.
- 5. (previously presented) The method of claim 3 in which only hydrogen-bond-donating and hydrogen-bond-accepting features are used.
- 6. (currently amended) A computer implemented method to search a <u>heterogeneous</u> heterogeneous compound database composed of molecules from different sources and syntheses, some known and some unknown, for molecular cores which are likely to have the same biological activity as a known query molecule core comprising the following steps:
 - a) specifying a known core and its two attachment bonds;
 - b) topomerically aligning the query core to generate a topomeric conformation;
 - c) generating the interaction energies between a probe and the atoms in the topomerically aligned query core at all intersection points in a three dimensional grid surrounding the aligned query core;
 - d) fragmenting database molecules into three fragments according to a defined set of

rules;

- e) topomerically aligning the central database molecule fragments generated by the fragmentation process of step (d) to generate a topomeric conformation;
- f) generating the interaction energies between a probe and the atoms in the topomerically aligned central database molecule fragments at all intersection points in a three dimensional grid surrounding the aligned central fragments;
- g) determining the similarity between query core and central database molecule fragments by the root sum square differences in the field values; and
- h) identifying the core in the database most similar to the query molecule core as that core having the smallest field value difference molecule; and
- d) outputting the identity of the core.
- 7. (previously presented) The method of claim 6 in which an attachment penalty multiplier is employed.
- 8. (new) The method of claim 1 in which the output displays the fragment of the best hits and the query fragment that it matches.
- 9. (new) The method of claim 2 in which the output displays the fragment of the best hits and the query fragment that it matches.
- 10. (new) The method of claim 3 in which the output displays the fragment of the best hits and the query fragment that it matches.
- 11. (new) The method of claim 4 in which the output displays the fragment of the best hits

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and the query fragment that it matches.

- 12. (new) The method of claim 5 in which the output displays the fragment of the best hits and the query fragment that it matches.
- 13. (new) The method of claim 6 in which the output displays the fragment of the best hits and the query fragment that it matches.
- 14. (new) The method of claim 7 in which the output displays the fragment of the best hits and the query fragment that it matches.